

**REMARKS**

**A. The Amendments and the Status of the Claims**

Claims 100, 127, and 412 have been amended to define the Applicants' invention with more precision and particularity. The claims, as amended, are supported by the specification and the original claims. No new matter has been added. Claims 1-99, 101, 103-126, 128-193, 201, 202, 204-209, 214-216, 229-293, 301, 302, 304-309, 330, 338-346, and 357-411 have been previously canceled without prejudice. Claims 100, 102, 127, 194-200, 203, 210-213, 217-228, 294-300, 303, 310-329, 331-337, 347-356, and 412 are pending.

**B. Rejection Under 35 U.S.C. § 112, Second Paragraph**

Claims 100, 102, 127, 194-200, 203, 210-213, 217-228, 294-300, 303, 310-329, 331-337, 347-356, and 412 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention (page 2 of the Office Action).

The Examiner has objected to the term "solid membrane" as used in claims 100, 127, and 412. By the present amendment, claims 100, 127, and 412 have been amended and the limitation "solid" have been deleted. Therefore, the rejection has become moot. Accordingly, the withdrawal of the rejection is respectfully requested.

**C. Priority**

The Examiner has used the effective priority date of May 1, 1996 for the examination of the present application (item 2 on page 2 of the Office Action). The Applicants submit that May 1, 1996 is an incorrect date. The correct priority date is June 7, 1995, for the following reasons. ✓

The present application is a continuation-in-part application of, and claims priority to, the U.S. Patent Application No. 08/497,684 ("parent application") having the filing date June 7, 1995. The priority was claimed when the present application was originally filed (page 1, lines 4-8 of the application, as originally filed). The priority is also reflected by the corrected filing receipt issued February 24, 1999 a copy of which is attached for the Examiner's easy reference.

It is, of course, required, that the co-pendency be maintained in a chain of applications claiming priority to one another. It is submitted that this requirement is satisfied as shown in the following chart reflecting the continuity data. As can be seen each child application in the chain was filed while the parent application was still pending.

**TABLE 1. THE CONTINUITY DATA FOR THE PRESENT FAMILY OF APPLICATIONS**

Application USSN	Filing Date	Status or Termination Date and Reason	Claims priority to USSN
09/218,660 (the present application)	12/22/98	Currently pending	08/660,032
08/660,032	06/06/96	Abandoned; the Notice of Abandonment dated 05/28/99	08/640,464
08/640,464	05/01/96	Abandoned; the Notice of Abandonment dated 07/17/97	08/497,684
08/497,684	06/07/95	Abandoned; the Notice of Abandonment dated 04/01/97	N/A

It is also axiomatic that a continuation-in-part application is entitled to the filing date of the parent application for the priority purposes, as long as every limitation of the claims of the continuation-in-part application is disclosed in the parent application. It is submitted that every feature and limitation recited in the claims of the present application are disclosed in the parent application, thus entitling the present application to the filing date of the parent application, i.e., June 7, 1995.

More specifically, the claims of the present application are directed to formulations that include a targeted vesicle having a membrane filled with a gas at room temperature. The parent application discloses such vesicles (e.g., on page 8, lines 4-5) filled with a gas (e.g., on page 15, lines 14-15). It is further recited in the claims of the present application that gas is selected from perfluorocarbons and sulfur hexafluoride. Using both perfluorocarbons and sulfur hexafluoride is disclosed in the parent application (page 16, lines 8-9 and claim 6).

The claims of the present application also require that the membrane contain a phospholipid, be free of disulfide linkages, and further include a conjugate comprising a lipid, a linking group and a targeting ligand. Using phospholipids is disclosed in the parent application (page 9, lines 16-17), as is using disulfide-free linkages (e.g., using amide, ester, thioester, ether, or amino linkages, as described on page 48, lines 20-24 and lines 34-36 of the parent application). Using a lipid-linking group-targeting ligand is also disclosed in the parent application (page 48, lines 12-18).

The claims of the present application also recite that the linking group is a hydrophilic polymer such as PEG, polypropylene glycol, etc. This limitation is disclosed on page 38, line 21 of the parent application (hydrophilic polymer in general) and on page 37, line 37 through page 38, line 8 (examples of specific hydrophilic polymers). Finally, the claims of the present application also recite the classes of targeting ligands such as proteins, peptides, etc. This limitation is disclosed on page 8, lines 9-15 and page 43, line 10 through page 44, line 18 of the parent application.

It is, therefore, clear that the claims of the present continuation-in-part application are fully supported by the disclosure of the parent application. Accordingly, it is submitted that the present application is entitled to the priority date of the parent application, i.e., June 7, 1995.

**D. Rejections Under 35 U.S.C. § 103(a)**

The Examiner rejected claims 100, 102, 127, 194-200, 203, 210-213, 217-220, 294-300, 303, 310-317, 326, and 412 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,620,689 to Allen, in view of U.S. Patent No. 4,853,228 to Wallach, U.S. Patent No. 5,643,553 to Schneider and U.S. Patent No. 5,648,098 to Porter (item 3 on pages 3-6 of the Office Action). The Examiner in addition rejected claims 318-325, 327-329, 331-337, and 347-356 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Allen, in view of Wallach, Schneider and Porter and further in view of U.S. patent No. 5,656,442 to Ginsburg (item 4 on pages 6-7 of the Office Action). These rejections are respectfully traversed.

To establish a *prima facie* case of obviousness, the following three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference(s) as proposed by the Examiner; (2) there must be a reasonable expectation of success and (3) the prior art reference(s) must teach or suggest all of the claim limitations. The Applicants respectfully submit that none of the criteria has been satisfied in this case because none of the cited references, either alone or in combination, disclose or suggest every limitation of claims 100, 127, and 412.

Specifically, each of claims 100, 127, and 412, recites vesicles "gas-filled vesicles" wherein the gas is a "perfluorocarbon or sulfur hexafluoride." The references cited by the Examiner do not disclose such limitations. As correctly pointed out by the Examiner (page 4, last line of the Office Action), Allen does not teach gas-containing vesicles. As also noted by the Examiner (page 5, lines 12-13 of the Office Action), Wallach fails to disclose a liposome containing a gaseous ultrasound agent. In addition,

the Examiner has also determined that Schneider fails to teach a perfluorinated gaseous liposome covalently bound to a targeting ligand (page 6, lines 2-3 of the Office Action). It can be added that Schneider is likewise silent with regard to using sulfur hexafluoride gaseous liposome covalently bound to a targeting ligand. With respect to the Ginsburg reference, Ginsburg fails to cure this deficiency, Ginsburg describes specific targeting agent, but does not disclose using gas-filled vesicles.

Not only do Allen, Wallach, Schneider or Ginsburg, or any combination thereof, fail to explicitly disclose vesicles perfluorocarbon or sulfur hexafluoride-filled vesicles covalently bound to a targeting ligand, it is submitted that there is nothing in Allen, Wallach, Schneider or Ginsburg, or any combination thereof, providing suggestion that might motivate one skilled in the art to prepare such formulation. These references are simply silent in that regard.

Therefore, a combination Allen, Wallach, Schneider, or Ginsburg fails to teach or suggest every element of claims 100, 127, or 412. The Examiner proposed to use the disclosure of Porter teaching the use of perfluorocarbons to cure the deficiency of the combination of Allen, Wallach, and Schneider or a combination of Allen, Wallach, Schneider, and Ginsburg. However, Porter is not available as the proper prior art reference.

It is well established that a 35 U.S.C. § 103 rejection must be based on a subsection of 35 U.S.C. § 102. See, MPEP § 2141.01. In other words, to qualify as a valid 35 U.S.C. § 103 reference, the reference must also qualify as prior art under a section of 35 U.S.C. § 102. See, *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir. 1987).

As discussed above, the present application has the priority date June 7, 1995. The earliest reference date for Porter is October 17, 1995, its filing date. Therefore, the present application pre-dates Porter, and accordingly Porter is not prior art against the present application, and thus does not qualify as a valid 35 U.S.C. § 103 reference.

In re Application of:  
Unger et al.  
Application No.: 09/218,660  
Filed: December 22, 1998  
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PATENT  
Attorney Docket No.: IMARX1100-3

In view of the foregoing, it is respectfully submitted that claims 100, 127 and 412 are patentably distinguishable over the references cited by the Examiner. All other claims depend, directly or indirectly, on either claim 100 or claim 127, and are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

In re Application of:  
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PATENT  
Attorney Docket No.: IMARX1100-3

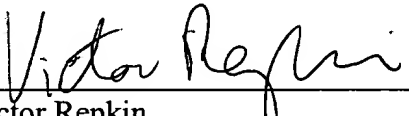
**CONCLUSION**

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

No fee is believed due in connection with this response. In the event that an additional fee is due, the Commissioner is hereby authorized to charge any amounts required by this filing, or credit any overpayment, to Deposit Account No. 07-1896.

Respectfully submitted,

Date: September 28, 2005

  
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FILING RECEIPT  
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UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
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Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.	DRWGS	TOT CL	IND CL
09/218,660	12/22/98	1616	\$2,392.00	UNGR-1520	4	193	13

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Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Application Processing Division's Customer Correction Branch within 10 days of receipt. Please provide a copy of the Filing Receipt with the changes noted thereon.

Applicant(s)

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CONTINUING DATA AS CLAIMED BY APPLICANT-

THIS APPLN IS A CIP OF 08/660,032 06/06/96  
WHICH IS A CIP OF 08/640,464 05/01/96 ABN  
WHICH IS A CIP OF 08/497,684 06/07/95 ABN

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\* SMALL ENTITY \*

TITLE

NOVEL TARGETED COMPOSITIONS FOR DIAGNOSTIC AND THERAPEUTIC USE

PRELIMINARY CLASS: 424

ENTRY BY: HINES, BRENDA

TEAM: 06 DATE: 02/24/99

(see reverse)